



Synthesis, Structural Characterization and DNA Binding Studies on Transition Metal Complexes with 2-Formylpyridine Benzoylhydrazone

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The hydrazone ligand, 2-formylpyridine benzoylhydrazone (FPBH) has been used to synthesize copper(II), nickel(II) and cobalt(II) complexes and characterized by elemental analyses, mass spectra, molar conductivity data IR, UV-visible spectroscopy. The complexes are found to have general formula $M(\text{FPBH})_2$ (where, $M = \text{Cu(II)}, \text{Ni(II)}$ and Co(II)). Further the copper complex is investigated using ESR spectra. The spin Hamiltonian, orbital reduction and bonding parameters are calculated for the complex. The complex, $\text{Ni}(\text{FPBH})_2$ is structurally characterized based on single crystal X-ray crystallography. The complex crystallizes in monoclinic space group $P21/c$ with $a = 11.2632(2) \text{ \AA}$, $b = 8.8958(2) \text{ \AA}$, $c = 23.0834(5) \text{ \AA}$, $\alpha = 90^\circ$, $\beta = 90.858(2)^\circ$, $\gamma = 90^\circ$, $V = 2312.59(8) \text{ \AA}^3$ and $Z = 4$ with central Ni(II) ion in distorted octahedral structure coordinated by two tridentate FPBH ligand. The interactions of these complexes with calf thymus DNA have been investigated using absorption spectrophotometry. The copper complex binds more strongly than either nickel or cobalt complexes.

Keywords: Transition metal(II) complexes, Hydrazone ligand, DNA binding.

INTRODUCTION

DNA is the storage site of cellular information. It is accessed continuously for storing and dispensing information required for existence. Thus, it acts as the main intracellular target for those who thrive to develop a new drug for innumerable diseases, especially cancer. It is known that small molecules that can bind and react with specific DNA sites provide a means to access and manipulate this cellular information creating the desired results. There are many binding modes by which the small molecules bind to the DNA which are covalent and non-covalent binding. Cisplatin binds covalently with the DNA thereby restricting its replication. Non-covalent binding modes are intercalation, groove binding and external electrostatic binding. Among the non-covalent binding modes, intercalation is the most important one because it invariably leads to cellular degradation [1].

During the last decade many reports are available throughout the literature regarding the interactions of transition metal complexes with DNA. Metal complexes have been used as tools for understanding DNA structure, as agents for mediation of DNA or as chemotherapeutic agents. Metal complexes

provide an opportunity to explore the effects of central metal atom, the ligands and the coordination geometries on the binding event. Moreover, the activity of complex depends on binding ability to DNA strands [2-4]. Platinum based complexes had been primary focus of research on chemotherapy agents [5-7]. Since platinum complexes are expensive and show side effects, the interests in this field have been shifted to non-platinum based agents. Essential transition metal complexes appear to be very promising agents for anticancer therapy having effective cytotoxic activities [8-11]. The literature survey indicates that the pharmacological activity depends on the nature of metal ion, organic scaffold and specific DNA binding site [12].

Tridentate hydrazones having assorted donor atoms are efficient ligands in coordinating with metal ions to form complexes having specific geometry. Such complexes serve as models for metallo proteins containing active sites [13-17].

A number of transition metal complexes of hydrazones have been reported [18], but there are few reports available in the literature on DNA binding of such complexes. Copper(II) and zinc(II) complexes with 2-benzoylpyridine-methylhydrazone are reported by Beraldo *et al.* [19]. Koo *et al.* [20] reported

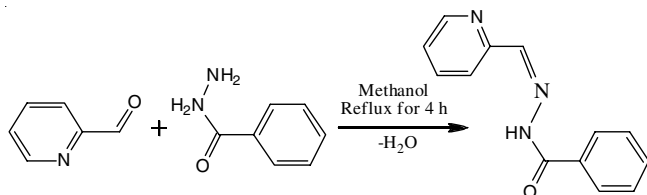
Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes of 2-acetylpyridine benzoylhydrazone. Recently we have reported [21-24] lanthanide complexes of 2-benzoylpyridine benzoylhydrazone, 2-acetylpyridine acetylhydrazone, 2-benzoylpyridine acetylhydrazone and 2-formylpyridine benzoylhydrazone. But there is no report on transition metal complexes with 2-formylpyridine benzoylhydrazone.

In the light of the above and in continuation of our studies on transition metal complexes of tridentate ligands and metal-DNA interactions [25-28], herein we report the synthesis structural characterization and DNA binding properties of copper(II), nickel(II) and cobalt(II) complexes with 2-formylpyridine benzoylhydrazone. Single crystal X-ray structure determination of Ni(FPBH)₂ complex is reported in this article.

EXPERIMENTAL

The chemicals used in the preparation of ligand, 2-formylpyridine benzoylhydrazone were of reagent grade (Aldrich) and were used without further purification Metal salts used in the synthesis of complexes were of reagent grade (Merck). Solvents used in the present study were distilled before use. Calf thymus DNA was purchased from Genie Bio labs, Bangalore, India. All other chemicals were of AR grade and used without purification.

Synthesis of ligand 2-formylpyridine benzoylhydrazone (FPBH): The ligand was prepared [29] by condensation of a 2-formylpyridine (0.475 mL, 5 mmol) with benzhydrazide (5 mmol) in ethanol solvent. A 1.36 g of benzhydrazide (10 mmol) dissolved in 30 mL of ethanol were added to ethanolic solution (30 mL) 10 mmol of 2-formylpyridine (1.0 mL). The contents were refluxed over water bath for 1 h. The contents were cooled. On slow evaporation of solvent a yellow coloured product was formed. It was collected by filtration, washed with methanol and dried in vacuum. Preparation of FPBH ligand is shown in Scheme-I.



Scheme-I: Preparation of FPBH ligand

Synthesis of metal complexes: All the metal complexes were prepared by mixing hot methanolic solution (20 mL) of FPBH (1 g 0.55 mmol) and metal salt (CuCl₂·2H₂O/NiCl₂·6H₂O/CoCl₂·6H₂O; 0.55 mmol) dissolved in methanol (20 mL) in 1:1 ratio in a clean 100 mL round bottom flask and the contents were refluxed on water bath for 3 h. The resulting solution

was allowed to stand at room temperature and after slow evaporation, coloured complex, which separated out was collected by filtration, washed with methanol followed by hexane and dried *in vacuo*.

Physical measurements: The conductivity measurements at 298 ± 2 °C in dry and purified DMF were carried out on CM model 162 conductivity cell (ELICO). ESI-Mass spectral data were obtained from Karunya Institute of Technology and Sciences, Coimbatore, India. The electronic spectra of metal complexes were recorded in DMF with an ELICO spectrophotometer. The infrared spectra were recorded in the range 4000-400 cm⁻¹ with Perkin Elmer spectrum 100 spectrometer in KBr discs. ESR spectra were recorded in solid state and in DMF at 298 K and at liquid nitrogen temperature (LNT) on a Varian E-112 spectrometer with 100 KHz field modulation. The g_{||} and g_⊥ values are computed from the spectrum using tetracyanoethylene (TCNE) free radical as 'g' marker.

X-ray crystallography: X-ray crystallographic data and cell refinement parameters were collected on Enraf Nonius CAD4-MV31 diffractometer, (SAIF-IIT Madras) using graphite monochromated MoK α radiation at room temperature 293 K. The data collected were reduced using the SAINT program [30]. The structure was resolved by direct method using SHELXS-86 [31] and refined by full-matrix least square on F² (SHELXL-97) [32]. The graphic tool used was DIAMOND for windows [33]. ORTEP3 [34] were used to generate the ORTEP diagram.

DNA binding experiments: DNA binding experiments were done in *tris*-buffer (0.5 mM NaCl/5 mM *Tris*-HCl; pH = 7.0). A solution of CT-DNA in the buffer medium gave a ratio of UV absorbance at 260 and 280 nm (A₂₆₀/A₂₈₀) of 1.8-1.9, indicating that the CT-DNA was apparently free of proteins. Concentration of CT-DNA was estimated by using the ϵ value of 6600 M⁻¹ cm⁻¹ at 260 nm and stock solution of DNA was always stored at 4 °C. The electronic spectra of metal complexes in aqueous solutions were monitored in the absence and presence of CT-DNA. Absorption titrations were performed by maintaining the metal complex concentration 10 × 10⁻⁶ M and varying the nucleic acid concentration (0 to 7.36 × 10⁻⁶ M). Absorption titration experiments were performed by varying the concentration of CT-DNA with each addition of 10 μ L DNA while the fixed metal complex concentration. The ratio of r = [complex]/[DNA] values vary from 23.41 to 2.60.

RESULTS AND DISCUSSION

The reaction of FPBH with metal chlorides yielded in the formation of mononuclear complexes. All the complexes are non-hygroscopic, coloured and freely soluble in ethanol and soluble in many organic solvents. Physico-chemical and analytical data of complexes are given in Table-1. Mass spectra of

TABLE-1
PHYSICO-CHEMICAL AND ANALYTICAL DATA OF Cu(II), Ni(II) AND Co(II) COMPLEXES

| Complex | Colour | Yield (%) | m.w. | Elemental analysis (%): Found (calcd.) | | | | Molar conductivity (Ω^{-1} cm ² mol ⁻¹) |
|-----------------------|--------|-----------|------|--|-------------|---------------|---------------|--|
| | | | | C | H | N | M | |
| Cu(FPBH) ₂ | Green | 79 | 512 | 51.72 (51.56) | 4.25 (4.29) | 16.73 (16.40) | 12.50 (12.41) | 10.4 |
| Ni(FPBH) ₂ | Brown | 70 | 507 | 61.36 (61.53) | 4.30 (4.33) | 16.45 (16.56) | 11.65 (11.57) | 6.5 |
| Co(FPBH) ₂ | Brown | 60 | 507 | 61.45 (61.53) | 4.40 (4.33) | 16.70 (16.56) | 11.25 (11.62) | 6.1 |

Cu(FPBH)₂; Cu(FPBH)₂ and X-ray data for Ni(FPBH)₂ are consistent formula proposed for the complexes. Molar conductivity data of the complexes suggest non-electrolytic [35] nature of complexes.

Spectral characterization: The electronic spectrum of copper complex is dominated by intense charge transfer bands at 33,898 cm⁻¹. The presence of a single *d-d* band at 13,586 cm⁻¹ may be assigned symmetric nature of ligand field and is assigned to ²E_g → ²T_{2g} electronic transition in favour of octahedral structure. The electronic spectrum of nickel complex (Fig. 1) shows bands at 27855 (ν₃), 11627 (ν₂) and 9500 (ν₁) cm⁻¹.

These peaks are assigned to ³A_{2g}(F) → ³T_{2g}(F), ³A_{2g}(F) → ³T_{1g}(F) and ³A_{2g}(F) → ³T_{12g}(P) transitions respectively. The spectral data are used to compute important ligand field parameters using ligand field theory of spin allowed transitions in *d*⁸ configuration. The ligand field parameters like field splitting energy (10 Dq, 9500 cm⁻¹), Racah interelectronic repulsion parameters (B', 732 cm⁻¹) and nephelauxetic ratio (β, 0.693) and ligand field stabilization energy (27.14 KJ) and percentage of covalent character (30.7) have been calculated. The β value is less than unity suggesting considerable amount of covalent character in M-L band. Electronic spectrum of

cobalt complex shows distinct bands at 16,501 and 14814 cm⁻¹ attributable to ⁴T_{1g}(F) → ⁴A_{2g}(F) (ν₂) and ⁴T_{1g}(F) → ⁴T_{2g}(P) (ν₃) transition respectively in favour of octahedral structure.

ESR spectra of copper complex: ESR spectrum of Cu(FPBH)₂ complex in DMF at room temperature (RT) is shown in Fig. 2a. ESR spectral data of complexes in solid state and in DMF are given in Table-2. The *g* values were computed from the spectrum using tetracyanoethylene (TCNE) free radical as the *g* marker.

At room temperature: The *g*_{||} and *g*_⊥ values for Cu(FPBH)₂ complexes are respectively found to be 2.12 and 2.05 in DMF at room temperature. Kivelson and Neiman [36] have reported that the *g*_{||} is less than 2.3 for covalent character and greater than 2.3 for ionic character of the metal-ligand bonding. The *g*_{||} value suggests covalent character for the complex. The trend, *g*_{||} > *g*_⊥ > 2.0023 suggest that the unpaired electron predominantly in the *d*_{x²-y² orbital [37] characteristic of octahedral geometry for copper(II) complex.}

The *g*_{av} value for the complex suggest the presence of covalent character [38] in M-L bond. The axial symmetry parameter *G* is defined as:

$$G = \frac{[g_{||} - 2.0023]}{[g_{\perp} - 2.0023]}$$

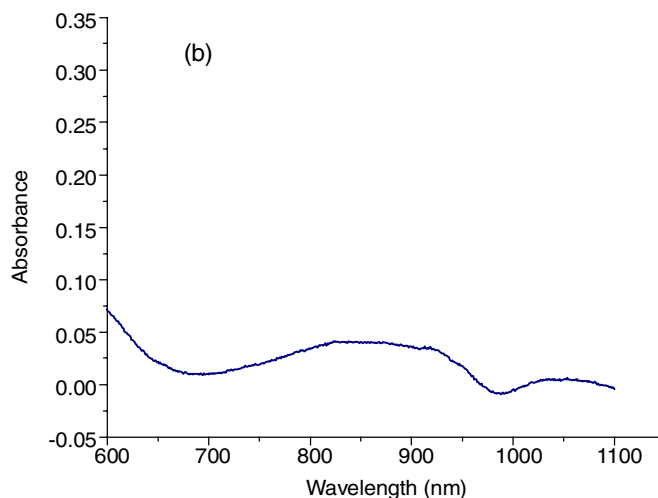
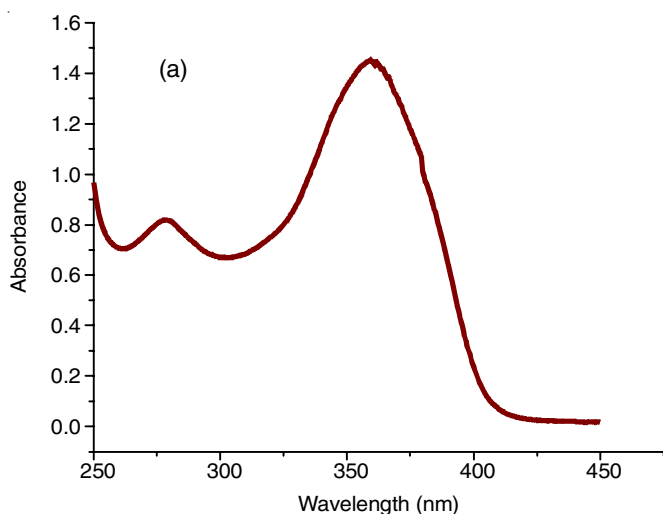


Fig. 1. Electronic spectra of Ni(FPBH)₂ complex (a) at low concentration and (b) at high concentration

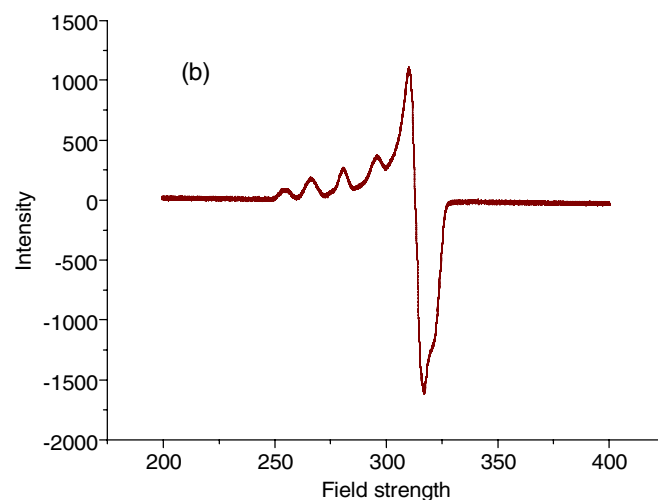
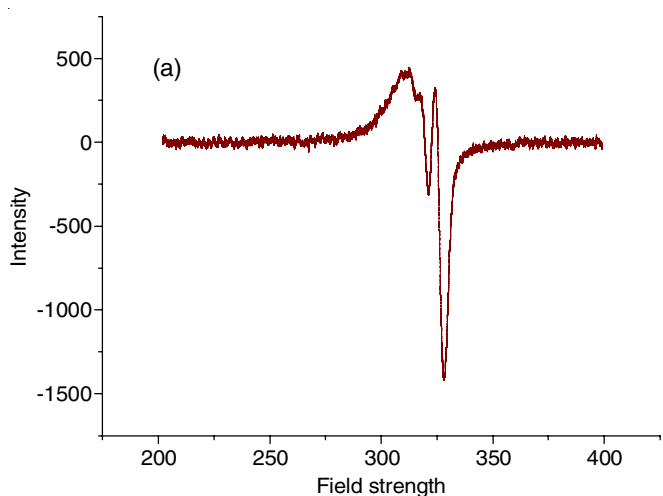


Fig. 2. ESR spectra of Cu(FPBH)₂ complex (a) at room temperature and (b) at liquid nitrogen temperature

TABLE-2
ESR DATA, SPIN HAMILTONIAN AND ORBITAL
REDUCTION PARAMETERS OF Cu(FPBH)₂ COMPLEX

| Parameter | Value at liquid nitrogen temperature | Value at room temperature |
|--------------------------------|--------------------------------------|---------------------------|
| g_{\parallel} | 2.32 | 2.12 |
| g_{\perp} | 2.03 | 2.05 |
| g_{ave} | 2.17 | 2.07 |
| G | 10.94 | 2.36 |
| $A_{\parallel} \times 10^{-5}$ | 0.00129 | – |
| $A_{\perp} \times 10^{-5}$ | 0.0004 | – |
| K_{\parallel} | 0.991 | – |
| K_{\perp} | 0.581 | – |
| λ | 546 | – |
| α^2 | 0.33 | – |
| p | 0.0013 | – |

The calculated G value for Cu(FPBH)₂ complex is found to be 2.36. The G value is less than 4 for Cu(FPBH)₂ complex indicates the absence of exchange coupling and misalignment of molecular axes.

At liquid nitrogen temperature: The typical ESR spectrum of Cu(FPBH)₂ complex in DMF at liquid nitrogen temperature (LNT) is shown in Fig. 2b. ESR spectra of complexes in DMF at liquid nitrogen temperature (LNT) exhibit well resolved peaks at low field and at high field corresponding to g_{\parallel} and g_{\perp} respectively.

The spin Hamiltonian, orbital reduction and bonding parameters of complexes are incorporated in Table-2. The A_{\parallel} and A_{\perp} are the separation between two adjacent g_{\parallel} and two adjacent g_{\perp} peaks respectively (cm^{-1}). The orbital reduction parameters (K_{\parallel} , K_{\perp}) are calculated using the following equations:

$$g_{\parallel} = g_e - \frac{8K_{\parallel}^2 \lambda}{\Delta E(d-d)}$$

$$g_{\perp} = g_e - \frac{2K_{\perp}^2 \lambda}{\Delta E(d-d)}$$

Hathaway pointed that for pure sigma bonding $K_{\parallel} = K_{\perp} = 0.77$ and for in-plane pi bonding $K_{\parallel} < K_{\perp}$, while for out-plane π -bonding $K_{\parallel} > K_{\perp}$. For Cu(FPBH)₂ complex, K_{\parallel} and K_{\perp} are 0.991 and 0.581, respectively. These values suggest the presence of out of plane π -bonding in the complex.

The factor α^2 , which is usually taken as a measure of covalency is evaluated by the following expression:

$$\alpha^2 = -A_{\parallel}/p + (g_{\parallel} - 2.0023) + 3/7(g_{\perp} - 2.0023) + 0.04$$

The α^2 value for the complex (0.34), suggest the covalent nature of metal ligand bond.

The dipolar term p is estimated from the expression:

$$p = (A_{\parallel} - A_{\perp})/(g_{\parallel} - 2.0023) - 5/14(g_{\perp} - 2.0023) - 6/7$$

Giordano and Bereman [39] suggest the identification of bonding groups from the values of dipolar term "p". The reduction of "p" value from the free ion value (0.036 cm^{-1}) may be attributed to the presence of covalent character of M-L bonding.

IR spectra: IR spectral data of hydrazone ligand are compared with those of metal complexes to determine donor atoms of ligand. Key IR spectral bands and their assignment are given in Table-3.

TABLE-3
KEY IR SPECTRAL BANDS (cm^{-1}) OF Cu(II),
Ni(II) AND Co(II) COMPLEXES OF 2-FORMYL
PYRIDINE BENZOYLHYDRAZONE (FPBH)

| Assignment | FPBH | Cu(FPBH) ₂ | Ni(FPBH) ₂ | Co(FPBH) ₂ |
|------------|------|-----------------------|-----------------------|-----------------------|
| $\nu(NH)$ | 3198 | – | – | – |
| $\nu(CH)$ | 3026 | 3026 | 3026 | 3025 |
| $\nu(C=O)$ | 1685 | – | – | – |
| $\nu(C=N)$ | 1642 | 1594 | 1588 | 1637 |
| $\nu(C-O)$ | – | 1225 | 1231 | 1282 |
| $\nu(M-O)$ | – | 554 | 539 | 594 |
| – | – | 470 | – | 469 |

The IR spectra of the ligands have several prominent bands due to $\nu(N-H)$, $\nu(C=O)$ and $\nu(C=N)$ stretching modes. The first two bands disappeared in spectra of complexes (due to enolization followed by complexation) and a new $\nu(C-O)$ band in the range 1051-1043 cm^{-1} is appeared. The $\nu(C=N)$ is shifted to lower frequency in the spectra of all complexes suggesting the involvement of azomethine nitrogen in chelation. IR data suggest that the ligands acts as mono basic tridentate ligands in all metal complexes. The non-ligand bands in 597-565 and 493-481 cm^{-1} regions are tentatively assigned to $\nu(M-O)$ and $\nu(M-N)$ vibrations respectively.

Based on physico-chemical and spectral data a general structure (Fig. 3) for complexes is proposed.

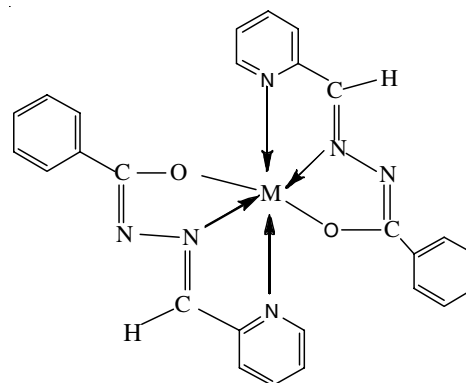


Fig. 3. A general and proposed structure for complexes of FPBH [where, M = Cu (II), Ni(II) and Co(II)]

Single crystal X-ray structure determination: The complex, Ni(FPBH)₂ crystallizes in monoclinic, space group P2₁/c. The structure refinement parameters are summarized in Table-4.

Important bond distances and bond angles are given in Table-5. ORTEP diagram of the complex is shown in Fig. 4.

The complex has 6-coordinate nickel. The structure of Ni(FPBH)₂ complex consists of two trifunctional monoanionic tridentate FPBH ligands, in which Ni(II) ion located on the two fold symmetry axis. The two ligand molecules coordinate the Ni(II) ion to form four five membered chelate rings [Ni-O₁-C₇-N₁-N₂; Ni-N₂-C₈-C₉-N₃; Ni-O₂-C₂-N₄-N₅; Ni-N₄-C₂₁-C₂₂-N₆]. The equatorial plane of Ni octahedron is defined by two acetyl pyridine ring nitrogen atoms and two oxygen atoms, while the axial positions are occupied by azomethine nitrogen atoms of each ligand molecule. This NiN₄O₂ coordination sphere is considerably distorted, which is probably due to the rigidity [40] of the ligand because of extended conjugation. The angles

TABLE-4
CRYSTAL DATA AND STRUCTURE
REFINEMENT FOR Ni(FPBH)₂ COMPLEX

| | |
|-----------------------------------|---|
| Empirical formula | C ₂₆ H ₂₀ N ₆ O ₂ Ni |
| Formula weight | 507.19 |
| Temperature | 296(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P2 ₁ /c |
| Unit cell dimensions | a = 11.2632(2) Å; α = 90° b = 8.8958(2) Å; β = 90.858(2)° c = 23.0834(5) Å; γ = 90° |
| Volume | 2312.59(8) Å ³ |
| Z | 4 |
| Density (calculated) | 1.457 Mg/m ³ |
| Absorption coefficient | 0.876 mm ⁻¹ |
| F(000) | 1048 |
| Crystal size | 0.150 × 0.150 × 0.100 mm ³ |
| Theta range for data collection | 3.056 to 25.000° |
| Index ranges | -13 ≤ h ≤ 13, -10 ≤ k ≤ 10, -27 ≤ l ≤ 27 |
| Reflections collected | 59106 |
| Independent reflections | 4069 [R(int) = 0.0379] |
| Completeness to θ = 25.000° | 99.7 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.7458 and 0.6844 |
| Refinement method | Full-matrix least-squares on F ² |
| Data/restraints/parameters | 4069/0/316 |
| Goodness-of-fit on F ² | 1.114 |
| Final R indices [I > 2σ(I)] | R1 = 0.0321, wR2 = 0.0927 |
| R indices (all data) | R1 = 0.0399, wR2 = 0.1009 |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.272 and -0.338 e.Å ⁻³ |

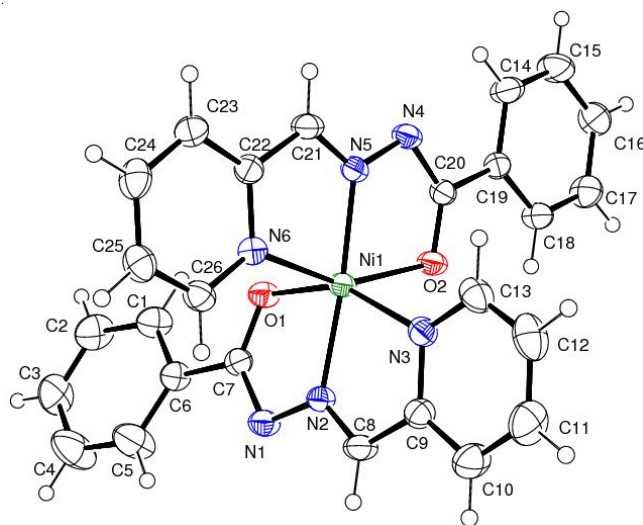


Fig. 4. ORTEP view of Ni(FPBH)₂ complex

to greater trans influence of coordinated azomethine nitrogen moiety. The X-Ray crystal data confirm that the complex has distorted octahedral structure (Fig. 4). The relatively short N₁–N₂ (1.372 Å) and N₄–N₅ (1.364 Å) bond lengths (normal single bond length is 1.52 Å coupled with lengthened C–O distance of 1.2685 Å indicates that the ligand acts as enol form. The ketonic C–O bond length is 1.23 Å.

Hydrogen bonding data for the structure of Ni(FPBH)₂ complex (Å and °) are given in Table-6.

TABLE-6
HYDROGEN BONDS FOR Ni(FPBH)₂ COMPLEX (Å AND °)

| D–H...A | δ(D–H) | δ(H...A) | δ(D...A) | ∠(DHA) |
|----------------------|--------|----------|----------|--------|
| C(12)–H(12)...N(4)#1 | 0.93 | 2.61 | 3.481(3) | 156.1 |
| C(26)–H(26)...N(1)#2 | 0.93 | 2.60 | 3.264(3) | 128.8 |

TABLE-5
SELECTED BOND LENGTHS (Å) AND BOND
ANGLES (°) FOR THE STRUCTURE OF Ni(FPBH)₂

| Bond | Angle (°) | Bond | Angle (°) |
|-----------------|------------|-----------------|------------|
| N(2)–Ni(1)–N(5) | 175.57(8) | O(1)–Ni(1)–N(6) | 92.98(7) |
| N(2)–Ni(1)–O(1) | 76.36(7) | O(2)–Ni(1)–N(6) | 154.06(7) |
| N(5)–Ni(1)–O(1) | 100.21(7) | N(2)–Ni(1)–N(3) | 77.80(7) |
| N(2)–Ni(1)–O(2) | 106.68(7) | N(5)–Ni(1)–N(3) | 105.75(7) |
| N(5)–Ni(1)–O(2) | 76.07(7) | O(1)–Ni(1)–N(3) | 153.98(7) |
| O(1)–Ni(1)–O(2) | 92.28(6) | O(2)–Ni(1)–N(3) | 92.20(7) |
| N(2)–Ni(1)–N(6) | 99.25(7) | N(6)–Ni(1)–N(3) | 94.11(7) |
| N(5)–Ni(1)–N(6) | 78.00(7) | | |
| Bond | Length (Å) | Bond | Length (Å) |
| Ni–N(2) | 1.9885(18) | Ni–N(6) | 2.1303(19) |
| Ni–N(3) | 2.149(2) | Ni–O(1) | 2.0816(16) |
| Ni–N(5) | 1.9893(19) | Ni–O(2) | 2.1118(16) |

at the Ni center show large deviation (Table-5) from ideal octahedral values of 90° and 180°. The tridentate ligands in the complex is almost planar. The three individual rings, namely the formylpyridine and the two five membered chelate rings, are individually nearly planar with small dihedral angles 21.02(7)°. The pair of coordinating ligands are nearly orthogonal to each other with the dihedral angles 87.92 (2)°.

The average bond distances for each Ni–O and Ni–N in this coordination geometry are 2.0967 and 2.064 Å respectively. The values are similar to that of typical Ni(II) complexes [41]. Equatorial Ni–N (formylpyridine) bond lengths are longer than axial Ni–N (>C=N- moiety) bond lengths, which can be related

Figs. 5 and 6 show packing of the molecule indicating non-covalent interactions.

DNA binding studies: UV-visible spectroscopy is an important technique to investigate the interaction of DNA with metal complexes. Hence the interaction of metal complexes with calf-thymus DNA was monitored by UV-visible spectroscopy. Absorption spectra were recorded in the range of 250–500 nm. Typical absorption spectra of in presence and in absence of DNA are shown in Fig. 7.

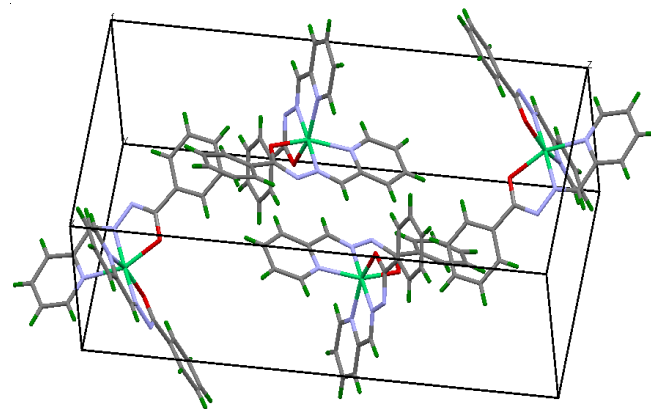
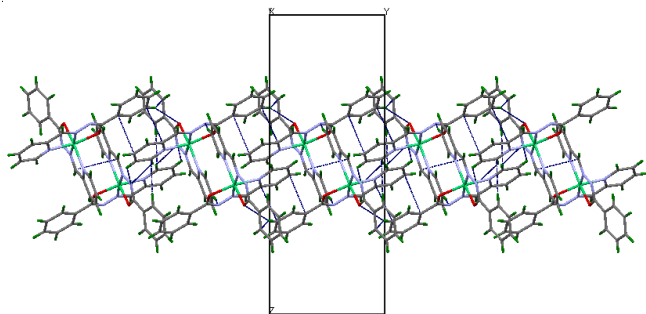


Fig. 5. Close packing of molecules of Ni(FPBH)₂ complex

Fig. 6. 1D and close packing view of Ni(FPBH)₂ complex

Metal complexes exhibit an intense absorption band in high energy region (345-395 nm) which are attributed to metal-ligand charge transfer (MLCT) transitions. The absorption spectra of complexes were compared in the absence and in the presence of CT-DNA. The change in absorbance values with increasing amounts of CT-DNA was used to evaluate the intrinsic binding constant K_b , for the complexes. Based on the variation in absorption, the intrinsic binding constant or association constant (K_b) of the metal complex can be calculated according to the Benesi-Hildebrand equation, modified by Wolfe *et al.* [42].

$$\frac{[\text{DNA}]}{(\epsilon_a - \epsilon_f)} = \frac{[\text{DNA}]}{(\epsilon_b - \epsilon_f)} + \frac{1}{K_b (\epsilon_b - \epsilon_f)}$$

where, ϵ_a , ϵ_f and ϵ_b correspond to $A_{\text{observed}}/[\text{complex}]$, the extinction coefficient for the free metal complex and the extinction coefficient for the metal complex fully bound to DNA, respectively, K_b represents the binding constant.

Electronic absorption spectral data upon addition of CT-DNA and binding constants of these complexes are given in Table-7.

In the presence of increasing amounts of CT-DNA, the UV-visible absorption spectra of metal complexes show a small bathochromic shift (red shift) (λ_{max} : 0.5-1.0 nm) with increasing amounts of DNA. The calculated binding constants are found in the range $2.5\text{-}4.4 \times 10^5 \text{ M}^{-1}$.

Metal complexes binding to DNA through intercalation usually result in hypochromism and bathochromism or hypso-

TABLE-7
ELECTRONIC ABSORPTION DATA UPON
ADDITION OF CT-DNA TO COMPLEXES

| Complex | λ_{max} | | $\Delta\lambda$ | H (%) | K_b (M^{-1}) |
|-----------------------|------------------------|-------|-----------------|--------|------------------------------|
| | Free | Bound | | | |
| Cu(FPBH) ₂ | 355.0 | 356.0 | 1.0 | +23.03 | 4.4×10^5 |
| Ni(FPBH) ₂ | 395.0 | 395.5 | 0.5 | +20.07 | 3.0×10^5 |
| Co(FPBH) ₂ | 345.5 | 346.5 | 1.0 | +32.06 | 2.5×10^5 |

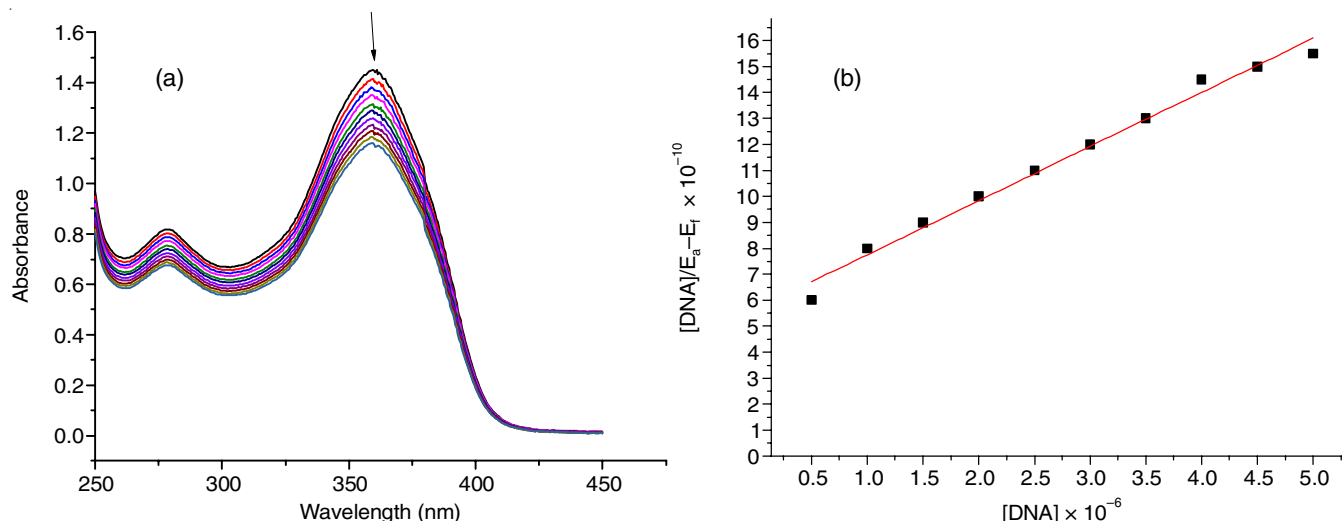
chromism [43-45] while hyperchromism has been attributed to electrostatic attraction, hydrogen bonding and groove (minor or major) binding along the outside of DNA helix [44,46,47]. The extent of the changes that appear in metal complex spectrum are usually consistent with strength of interaction that takes place. Such small bathochromic shifts is more inkeeping with groove binding, leading to small perturbations. The K_b values here are lower than that reported for classical intercalator for ethidium bromide and $[\text{Ru}(\text{Phen})_2\text{DPPZ}]^{2+}$ complex whose binding constants have been found to be in the order $10^6\text{-}10^7$ [48,49]. The observed binding constants for the present complexes are in accordance with groove binding with DNA as reported in the literature [50,51]. It is pertinent to note that the binding constant for Cu(FPBH)₂ complex is quite high. The increasing order of binding constant is found as shown below:



The above order suggest that the Cu(FPBH)₂ complexes binds DNA strongly.

Conclusion

Copper(II), nickel(II) and cobalt(II) complexes of 2-formylpyridine benzoylhydrazone (FPBH) have been synthesized and characterized based on physico-chemical and spectral data. The nickel complex is structurally characterized using single crystal X-ray crystallography. The complex is found to have distorted octahedral structure with the central Ni(II) ion coordinated by two tridentate FPBH ligand. The copper complex is investigated using ESR spectra. Groove binding of complexes to DNA is suggested based on binding constants and the variations in the absorption spectra of metal complexes in the presence of DNA.

Fig. 7. (a) Absorption spectra of Cu(FPBH)₂ complex in the absence and in the presence of increasing amounts of CT-DNA and (b) A plot between $[\text{DNA}]/(\epsilon_a - \epsilon_f)$ versus $[\text{DNA}]$

Supplementary information: Crystallographic data for the structure have been deposited with Cambridge Crystallographic Data centre (CCDC No. 1875483) copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 IEZ, UK (Fax: + 33-1223-336033 or main: deposit@ccdc.cam.ac.uk) or from authors upon request.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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